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PERIODONTAL SYNDROMIC ASSOCIATIONS - ADDRESSING GAPS IN KNOWLEDGE: A REVIEW

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ABSTRACT

The association between syndromes and periodontal disease is an interesting subject. Syndromes have widespread systemic manifestations throughout the body. The syndromes affecting the periodontium are not very common; hence they are missed on routine clinical diagnosis. Periodontium is affected by various syndromes and identification of periodontal manifestations plays a vital role in the diagnosis of syndromes itself. It is relevant to consider syndromes background to these severe periodontal cases, as it may eventually be relevant to treat and also to understand the pathogenesis of periodontitis in these patients.The knowledge of these syndromes is essential as they can influence the diagnosis, prognosis and management of periodontal disease. The aim of this review is to address how syndromes affecting the systemic health of an individual can also affect the periodontal health.

KEY WORDS: Periodontal manifestations, syndromes, systemic conditions.

Introduction

Periodontitis is a chronic infectious disease of the supporting tissues of the teeth. Due to bacterial infection, periodontal tissues become inflamed, and are gradually destroyed by the action of the inflammatory process.

The word syndrome is derived from the Greek word syn (together) and dromos (running) and refers to a 'running together' or concurrence of symptoms. Dorland's medical dictionary defines 'syndrome' as 'a set of symptoms that occur together, the sum of signs of any morbid state, a symptom complex'. In genetics, 'syndrome' refers to a pattern of multiple malformations that are thought to be pathogenetically related. The most relevant definition of a syndrome is provided by Cohen & Kreiborg, who stated that 'in medical genetics, a syndrome is recognized to represent multiple malformations occurring in embryonically noncontiguous areas.[1]

Syndrome is defined as the aggregate of signs and symptoms associated with any morbid process and constituting together the picture of the disease. Multiple manifestations may be related to common developmental or metabolic conditions. This poses a great challenge to the examiner to adequately diagnose and distinguish a syndrome from other pathologies. All syndromes have genetic components, and genetic disorders are inevitable which can affect everyone at some time.[2]

Identification of these syndromes and genetic counseling plays an important role.[2] As a result of unraveling of the complexities of genetic and phenotypic heterogeneities by newer genetic studies and methodologies, preventive strategies could be implemented in predisposed, susceptible individuals. If oral complications result from a syndrome and this can be anticipated, preventive measures can be initiated. If the risk of severe adverse outcomes is high, parent counseling about future pregnancies should be offered.

Is Periodontitis A Syndrome?

Based on a microscopic study of necropsy material, Thoma & Goldman described four types of periodontal disease, namely simple gingivitis, marginal periodontitis, paradontosis (generalized involvement), and syndromes of marginal periodontitis and paradontosis. Periodontal disease is labeled as a syndrome when referring to experimental studies in rice rats. According to van der Velden, a syndrome constitutes a distinct group of symptoms and signs that together form a characteristic clinical picture or entity. In this respect, periodontitis is a good example of a syndromically defined disease. He suggests that 'periodontitis must be regarded as a syndrome with a complex etiology' and states that when the etiology is not known or complex, a large number of diseases are defined as syndromes. Baelum and Lopez stated that "periodontal disease is a syndrome that comes in all sizes."[1]

However, not every disease that does not have a clear etiology can be called a syndrome. It has also been suggested that clinical conditions within the classification 'chronic periodontitis' are constellations of polymicrobial and polygenic infections whose clinical expression is profoundly altered by important environmental and host- modifying conditions. Such diverse clinical expressions probably give credence to the condition being called a syndrome. Since many syndromes affect the oral structures in a unique way, it aids in diagnosis.[1]

Involvement of periodontium in various syndromes

A study of the literature shows involvement of periodontal tissues in several syndromes. In certain situations, the association is strong, such as Down syndrome, Kindler syndrome and Kostman syndrome. . In some conditions, the periodontal findings are mere coincidence.[1]

In general syndromes could be **autosomal dominant, autosomal recessive, x-linked or sex-linked.**

Autosomal dominant

A pattern of inheritance in which transmission of a dominant allele on an autosome causes a trait to be expressed. Males and females are affected with equal frequency.[2]

Autosomal recessive

A pattern of inheritance resulting from transmission of a recessive allele on an autosome. Males and females are affected with equal frequency.[2]

X-linked dominant

A pattern of inheritance in which the transmission of a dominant allele on the X-chromosome causes a characteristic to be manifested.[2]

X-linked recessive

A pattern of inheritance in which the transmission of a recessive allele on the X-chromosome results in a carrier state in female and characteristics of an abnormal condition in males.[2]

Sex-linked inheritance

The transmission to successive generations of traits that are due to alleles at gene loci on a sex chromosome.

Autosomal dominant syndromes with periodontal implications-

Acro-osteolysis, Cowden syndrome, cyclic neutropenia, Down's syndrome, epidermal nevus syndrome, Ehlars Danlos syndrome (EDS), Feltys syndrome (FS), focal dermal hypoplasia (FDH), Francois syndrome, Gardeners syndrome hyperimmunoglobulin E syndrome, hypodontia and nail dysplastic syndrome, myelodysplastic syndrome, Sturge-Weber syndrome, tuberous sclerosis, and Zimmerman Laband syndrome.[2]

Sex-linked syndromes

Fragile-X syndrome, a problem with the FMR1gene on the X chromosome, which can cause mental retardation.

Autosomal recessive conditions

cystic fibrosis, sickle cell anemia, beta thalessemia

X-linked

Hypohidrotic ectodermal dysplasia

Syndromes associated with periodontal conditions like-
Gingival Enlargement
Gingival enlargement is one of the most common conditions seen by a clinician. While most gingival enlargement cases are minor or mild in nature and correlate with local gingival disease, marked enlargement is often encountered that defies local explanation. Drug-induced enlargement accounts for a considerable number of cases. Even after giving due allowance for local inflammatory conditions and drug usage, sporadic cases have been reported that have a syndromic background.[1]

Gingival Fibromatosis
Gingival fibromatosis is a frequently encountered clinical situation. Clark discussed gingival fibromatosis and its related syndromes, Shashi reported the genetic heterogeneity of gingival fibromatosis on chromosome 2p, Trackman & Kantarci discussed connective tissue metabolism and gingival overgrowth, and Coletta & Graner presented a systematic review of the subject. Hakkinen & Csiszar discussed characteristic and putative pathogenic mechanisms of hereditary gingival fibromatosis.

Hereditary gingival fibromatosis sometimes manifests with unconnected, distant clinical characteristics of syndromic nature. Hypertrichosis, mental retardation, deafness, nail and finger abnormalities, aggressive periodontitis, supernumerary teeth and growth deficiency are some of the associated abnormalities. The co-existence of hereditary gingival fibromatosis and aggressive periodontitis has been speculated to be a possible new syndrome.

An important finding is mutation of the gene SOS-1 (Son of sevenless) that triggers hereditary gingival fibromatosis. The SOS gene encodes a protein that is reported to activate the RAS pathway, which is an important growth signal. When the SOS gene is not mutated, its product is involved in normal growth of healthy gums. Hereditary gingival fibromatosis resulting from the SOS-1 mutation was first reported by Hart et al. This was the first study to link a specific gene mutation to gingival overgrowth.

Syndromes causing generalized swellings
Familial gingival fibromatosis, Laband syndrome , Merkerlson Rosenthal syndrome, Cross syndrome, Murray Puretic-Drescher syndrome, Rutherford syndrome, Ramon Syndrome Focal Dermal Hypoplasia syndrome/ Goltz- Gorlin syndrome, Bourneville-Pringle syndrome and Cowden's syndrome.

Management: Patient is advised on oral hygiene. A surgical intervention such as gingivectomy is indicated when the gingival enlargement causes impairment of esthetics and interferes with function.[4]

Syndromes associated with gingival bleeding
Although the most common cause of gingival bleeding is gingival disease or periodontitis, a tendency to bleed occurs in several systemic and hematological disorders. The most notable of these systemic conditions include hemophilia, purpura and sometimes after prolonged use of the antiplatelet agents like aspirin and clopidogrel. The presence of unexplained gingival bleeding and bleeding that is not commensurate with local conditions should alert the clinician to the possibility of systemic disease in distant organs. Sturge-Webber syndrome, Klippel-Trenaunay-Weber syndrome, Chediak-Higashi syndrome are syndromes that are thought to predispose to gingival bleeding. The former two syndromes cause gingival bleeding because of vascular malformations, the latter causes gingival bleeding secondary to defects in platelets .

Management: Special emphasis should be given to the hematologic factors (bleeding tendencies) and vascular involvement (hemangiomata) which may significantly influence orodental management and anesthesia.[4]

Syndromes associated with White Lesions in the Gingiva
Focal palmoplantar and oral mucosa hyperkeratosis syndrome or hyperkeratosis and attached gingival hyperkeratosis is an unusual genetic disorder (autosomal dominant) characterized by oral mucosal and dermal hyperkeratosis and bone loss. Marked white hyperkeratosis of the attached gingiva, presenting clinically as leukoplakia is a consistent finding.

Management : Supportive retinoids may be helpful.[4]

Syndromes associated with Red Lesions in the Gingiva
Klippel-Trenauny-Weber syndro and Sturge-Webber syndrome (encephalotrigeminal angiomatosis) are two syndromes which manifest as capillary haemangiomas on the gingiva. They can also lead to localized gingival enlargement and gingival bleeding. Dentists must be careful during tooth extractions and periodontal surgery so as to avoid bleeding complications .[3]

Melkersson – Rosenthal syndrome consists of the triad of recurrent facial swelling, facial paralysis and fissured tongue. Gingival lesions are present as irregular, oedematous swelling, slightly erythematous, affecting mainly the anterior interdental papillae and free and attached gingiva.

Sjogren's syndrome is a relatively common, chronic autoimmune disorder in which chronic gingivitis localized or generalized due to xerostomia and/or Candida infection may occur.

Gingival lesions in Osler-Rendu-Weber syndrome/hereditary haemorrhagic telangiectasias appear as small, localized or multiple, bright red macules that characteristically disappear when pressure is applied. Gingival recurrent bleeding, usually, during or after tooth brushing, is frequent.

Management : Dentists must be careful during tooth extractions and periodontal surgery so as to avoid bleeding complications.[4]

Syndromes associated with periodontitis, alveolar bone loss and tooth loss
The extremely high prevalence of periodontal disease in patients with syndromes is a common feature in literature. Most such associations are seen in younger subjects, usually affecting both the deciduous and permanent dentitions. Severe periodontal disease with alveolar bone loss, mobility of teeth and premature loss of deciduous and/or permanent teeth is the most common symptom. Down syndrome is the most common and widely studied, with characteristic involvement of the mandibular anterior teeth. Periodontists are likely to have in their care more cases of Down syndrome than any other chromosomal anomalies

The two categories of disorders causing periodontal destruction can be grouped as Collagen disorders and Neutrophil defects.

Collagen disorders
The Ehlers–Danlos syndromes are a heterogeneous group of inherited connective tissue disorders characterized clinically by skin fragility, skin hyperextensibility, joint hypermobility, and excessive bruising. . Poor wound healing is a component of a number of subtypes of Ehlers–Danlos syndrome, and severe, early-onset periodontitis has been associated with two subtypes: Ehlers–Danlos syndrome type 4 and Ehlers–Danlos syndrome type[8,10].

Dental management: Prophylactic antibiotics may be given for relevant procedures. Dental visits of short duration are preferable to avoid causing iatrogenic problems in the temporal mandibular joints. Inferior alveolar nerve blocks should be given with great care to avoid causing hematoma. Forces used in orthodontic treatment should be lighter than usual, given the fragility of the periodontal ligament. Since relapse is frequent, a longer period of retention is necessary. It is extremely important to test blood coagulation values before proceeding with surgery.[4]

Neutrophil defects
Leukocyte alterations are the consequence of an imbalance between their formation in the bone marrow and subsequent elimination by the mononuclear phagocytic system. Factors that can modify leucopoiesis are varied and can lead to an alteration in the number of leukocytes or tumoral alterations of white cells.

a. Quantitative Neutrophil Defects
A relative deficiency in neutrophil number can dramatically increase susceptibility to infectious diseases. Quantitative defects can be at the bone marrow like in Kostman syndrome and Felty's syndrome or at the periphery as in Lazy leukocyte syndrome. Other syndromes associated with decreased neutrophil counts and periodontal destruction include Herman sky–Pudlak syndrome and Shwachman–Diamond syndrome. All syndromes present with wide spread and early periodontal tissue destruction.

Leukocyte adhesion deficiency syndrome (LAD) is of two sub types I and II. Here, the neutrophils are unable to migrate extravascularly. Acute gingival inflammation of the primary and permanent dentition, gingival proliferation, gingival recession, mobility of teeth and pathological migration are common clinical features.

Hyperimmunoglobulin E syndrome is a multisystem disorder inherited as an autosomal dominant trait that affects the dentition, the skeleton, connective tissues, and immune system. Over-retention of primary teeth in contrast with the early loss of primary teeth due to periodontitis seen in other disorders of host defenses, is seen.

The Papillon-Lefevre syndrome is described as a diffuse palmoplantar keratosis associated with aggressive periodontitis of both primary and permanent dentitions. A particular form of Papillon Lefevre syndrome has been named the Haim-Munk syndrome, and is also associated with early periodontal destruction.

Down's syndrome was named after the English physician who in 1866 characterized the appearance and behavior of these patients. Gingival hyperplasia can occur secondarily due to mouth breathing, poor hygiene, and local irritating factors. The gingivitis frequently progresses to generalized early periodontitis, which commences in the deciduous dentition and continues to affect the permanent dentition .

Another syndrome with severe gingivitis, ulcerations of the tongue and buccal mucosa, and early onset periodontitis leading to premature loss of both deciduous and permanent dentitions is the Chediak-Higashi syndrome. Bleeding problems arise because of organelle abnormalities within platelets that inhibit normal clot formation.

Other syndromes with qualitative neutrophil defects that could predispose to periodontal destruction include Kindler syndrome and Hypotrichosis osteolysis periodontitis palmoplantar keratoderma syndrome.

b. Qualitative Neutrophil Defects

These can be defects in rolling and adhesion (Leukocyte adhesion deficiency syndrome), defects in migration and chemotaxis (Hyperimmunoglobulin E syndrome, lazy leukocyte syndrome, Papillon-Lefvre syndrome, Down's syndrome, Kindler syndrome) and defects in phagocytosis and intracellular killing (Chediak Higashi syndrome).

Other syndromes with qualitative neutrophil defects that could predispose to periodontal destruction include Kindler syndrome and Hypotrichosis osteolysis periodontitis palmoplantar keratoderma syndrome.

Management

Conventional preventive measures such as the use of topical fluoride, fissure sealants, dietary advice and the promotion of oral health. When oral surgical procedures are anticipated, a platelet count of ≥50,000 cells/μL, absolute neutrophil count of ≥500 cells/μL, and haemoglobin concentration of ≥7 g/ dL, are recommended to assure hemostasis and reduce the risk of postoperative bacterial infection.[4]

Miscellaneous syndromes

Miscellaneous syndromes include those of viral etiology (AIDS), metabolic disturbances (metabolic syndrome, periodontitis–atherosclerosis syndrome, acute coronary syndrome), psychological disturbances (Munchausens syndrome), chromosomal disturbances (Klinefelter syndrome), endocrine imbalance, collagen disturbances, lichen planus, epilepsy, mucopolysaccharide disturbances etc. The possible relationship between metabolic syndrome and periodontal parameters is a significant avenue of research and is likely to lead to groundbreaking and novel preventive and treatment strategies in periodontics.

DISCUSSION

Periodontitis is a chronic bacterial infection of the supporting structures of the teeth. The host response to infection is an important factor in determining the extent and severity of periodontal disease. Systemic factors affect the normal immune and inflammatory mechanisms modifying periodontitis.[4]

A syndrome is the association of several clinically recognizable features, signs, symptoms, phenomena, or characteristics that often occur together so that the presence of one or more features alerts the health care provider to arrive at a definitive diagnosis and treatment plan. A syndrome can refer to the traits that suggest the presence of a disease or indicate a greater likelihood of developing the disease. Syndromes that affect the periodontium are very common, and hence they can influence the prognosis and management of periodontal disease. Many conditions may give rise to an increased prevalence, incidence or severity of gingivitis and periodontitis, but the majority of the cases reported in the literature are insufficient to make any definitive statements on causal links between certain syndromes and periodontitis as only case reports do exist.

Microbial dental plaque is the initiator of periodontal disease but the host defences play a major role in the disease initiation and progression. As certain syndrome show oral manifestations, it becomes important we carefully take a thorough history, know the manifestation and detect the disease at the earliest and take precautions during the dental treatment.[4]

CONCLUSION

Early diagnosis ensures successful treatment. It becomes necessary that we know the oral manifestations of the syndromes that affect the periodontium and arrive at a proper diagnosis and treatment planning. Its important to take a thorough history, know the manifestation and detect the disease at the earliest and take precautions during the dental treatment. It is imperativeto be familiar with the special management required for these patients, in which the dental treatment can affect the underlying cause of the disease. Future, epidemiological studies designed to assess the role of systemic conditions and disorders in periodontal disease are needed, particularly to refine experimental design and data analysis; to identify gaps in knowledge with respect to mechanisms of factors known to play a role in increasing susceptibility to periodontal disease; and to address gaps in knowledge of the correlation with the systemic conditions suspected of being related to periodontal disease.[3]

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